REMARKS

Formalities

Claims 59-71 were pending in the application. Claims 63-69 were allowed. Claims 59-62 and 71 have been canceled. Claim 70 has been amended. The amendments to the claims do not add or constitute new matter. Support for the amendments may be found throughout the specification and originally filed claims. More particularly, support for the amendment to claim 70 may be found, for example, at page 21, line 29 through page 23, line 2, of the specification.

The foregoing amendments are made solely to expedite prosecution of the instant application and properly respond to the final rejection, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 63-70 are pending in the instant application.

Rejection under 35 U.S.C. § 103

Claims 59-62 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over Mansour *et al.*, 1988, *Nature,* 336(24):348-352 ("Mansour"), in view of Schweickart *et al.*, 1994, *Genomics,* 23: 643-650 ("Schweickart"). Applicants respectfully traverse this rejection.

According to the Examiner, Mansour teaches a strategy for targeted disruption of the *hprt* and proto-oncogene *int-2* in mice embryonic stem cells, and subsequent generation of knockout mice. The disclosure of Mansour specifically relates to a general method for isolating embryonic stem cells containing a targeted mutation in an endogenous gene. More particularly, Mansour teaches the targeted disruption of the *hprt* gene and the proto-oncogene *int-2* in mouse embryonic stem cells by homologous recombination using targeting constructs specific for these genes.

Schweickart, as characterized by the Examiner, teaches the cloning of the human and mouse lymphoid-specific GPCR gene designated EBI1 (for Epstein-Barr induced 1), and provides the cloned coding sequence for this gene. Further, the Examiner asserts that Schweickart teaches that EBI1 is highly homologous to several members of the leukocyte chemotactic peptide receptor family and that its expression is specific to lymphoid organs.

Further, according to the Examiner, Schweickart teaches that EBI1 may play a role in lymphocyte growth, differentiation, activation, leukocyte trafficking, and in the extravasation of blood cells into sites of inflammation.

As a basis of the obviousness rejection under 35 U.S.C. § 103, the Examiner asserts that the ordinary artisan would have been motivated to make a lymphoid specific GPCR knockout targeting construct according to the methods of Mansour in order to study the precise role the lymphoid specific GPCR gene plays in lymphocyte growth and regulation suggested by Schweickart. Applicants previously argued that the combined references failed to teach all of the claim limitations, and specifically failed to teach the specific recited phenotype resulting from disruption of the lymphoid specific GPCR gene in a mouse using the claimed targeting construct. The Examiner has maintained that the resulting phenotype does not represent a true limitation because it does not affect the targeting construct structurally.

Applicants remain in disagreement with the Examiner's conclusions. Applicants submit that the phenotypic properties resulting from disruption of the lymphoid-specific GPCR gene using the claimed targeting construct show that the construct does posses properties that distinguish it from the subject matter described in the prior art references. However, Applicants have overcome this rejection by cancellation of claims 59-62.

As the rejection under 35 U.S.C. § 103 is no longer relevant, and claims 63-70 are not obvious in view of the sole or combined teachings of Mansour and/or Schweickart, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 70 and 71 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicants respectfully traverse this rejection.

Specifically, the Examiner asserts that claims 70 and 71 are incomplete for omitting essential steps, such omission amounting to a gap between the steps. The Examiner alleges that this omitted step is the selection of the ES cells that have undergone homologous recombination. Applicants disagree that the omission of this step amounts to a gap between steps, and submit that the method as recited in the previous version of the claim includes all steps regarded as the invention. The Examiner has further alleged that the phrase "wherein the pseudopregnant mouse gives birth" renders the claim indefinite because a pseudopregnant mouse cannot give birth.

Applicants also traverse this aspect of the rejection. Although Applicants disagree with the Examiner's conclusions and traverse the rejection, claim 70 has been amended to include the allegedly omitted step and recite that the "resultant mouse" and not a pseudopregnant mouse gives birth. Claim 71 has been canceled. Therefore, the rejection is no longer relevant, and Applicants respectfully request withdrawal of the rejection. .

Applicants submit that the pending claims are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

Claim Objections

Claim 71 has been objected to by the Examiner under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 68. The Applicants disagree. However, Applicants have overcome the objection by the cancellation of claim 71.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-611.

Respectfully submitted,

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